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Ectopic Pregnancy—Becoming a Nonsurgical Disorder

THE INCIDENCE OF ectopic pregnancy has been gradually rising, accounting for almost 2% of all pregnancies. Ectopic pregnancy has become a leading cause of maternal morbidity and mortality.[1]

Accurate and early diagnosis is essential for the appropriate use of conservative medical and surgical treatment of ectopic pregnancy.[2,3] In appropriate cases, expectant management may be an option. Ectopic pregnancy can become a "nonsurgical disorder" with early nonsurgical diagnosis and medical management with methotrexate in physicians' offices.[4] The effectiveness of methotrexate therapy is enhanced when given early (ectopic mass < 3.5 cm, no fetal cardiac activity, and human chorionic gonadotropin [hCG] level < 15,000 IU per liter [15,000 mIU per ml]).[5] Most women with ectopic pregnancy who are not candidates for methotrexate therapy can be treated surgically through the laparoscope on an outpatient basis.[6] Laparotomy and hospital admission will be necessary in a few patients who are hemodynamically unstable. In addition to minimizing surgical intervention, early diagnosis and treatment may improve fertility following ectopic pregnancy. The cost savings of early diagnosis and treatment could be enormous. Outpatient methotrexate treatment could cost as little as $500 compared with $5,000 to $15,000 for surgical treatment.

Patients with ectopic pregnancies still present with tubal rupture and compromised hemodynamic status and consequently require emergency laparotomy. Both patients and medical staff must be better educated. No diagnostic test is useful until it is ordered. For women who have risk factors for ectopic pregnancy, there must be a high degree of suspicion in the presence of abnormal vaginal bleeding and abdominal pain. A sensitive hCG assay must be done as soon as pregnancy is suspected. Primary care and emergency department physicians must also have a high degree of suspicion and diligently observe high-risk patients during early pregnancy.

A single quantitation of hCG cannot be used to separate ectopic versus normal pregnancies unless correlated with an ultrasonogram of the pelvis. The major value of hCG levels is in establishing discriminatory zones when ultrasonography can be used to rule out intrauterine pregnancy. Physicians must establish their own discriminatory zone. Factors affecting minimum values of hCG needed to visualize an intrauterine pregnancy include the reference standard for hCG levels, abdominal versus vaginal ultrasonography,[7] and ultrasonographic experience. Serial quantitative hCG titers have become the standard for assessing viability in early pregnancy, with a rate of rise of less than 66% over 48 hours in most nonviable pregnancies. Because as many as 20% of ectopic pregnancies can have normally rising hCG titers, serial hCG titers are often used to determine when a discriminatory level of hCG is reached to appropriately time an ultrasound examination. Extra care is needed to interpret hCG values in patients at high risk for multiple pregnancy (ovulation induction and in vitro fertilization). The demise of one twin may result in temporary plateauing or falling of hCG levels with the remaining twin surviving.

Ultrasonography is used most often to exclude ectopic pregnancy by diagnosing an intrauterine gestational sac; the likelihood of both an intrauterine and ectopic pregnancy is only 1 in 30,000. As ultrasound technology and skill improve, an increasing number of ectopic pregnancies (as many as 70%) can be visualized by ultrasonography. Vaginal sonography has lowered the discriminatory zone for hCG (1,000 to 2,000 IU per liter for vaginal and 6,000 to 6,500 IU per liter for abdominal), thus lowering the gestational age at diagnosis. Vaginal sonography is also used to assess additional adnexal disorders (ovarian cysts and hydrosalpinx), the presence of fluid in the peritoneal cavity, the presence of fetal cardiac activity, and the size of the ectopic pregnancy. All of these sonographic findings will influence the selection of appropriate treatment.

Because serial hCG assessment results in a 48-hour delay in the diagnosis, the single assessment of serum progesterone concentrations has been used to assess fetal viability. A high predictive value is associated with progesterone values of more than 80 nmol per liter (25 ng per ml) for viable and less than 16 nmol per liter (5 ng per ml) for nonviable fetuses.[8] Patients with progesterone concentrations of less than 80 nmol per liter may benefit from ultrasonic evaluation to increase the likelihood of the early diagnosis of ectopic pregnancy. Because of considerable assay variation, each laboratory will have to establish its own threshold values. The progesterone level is of little value in differentiating early miscarriage from ectopic pregnancy.

There may be no role for culdocentesis in the contemporary diagnosis and management of ectopic pregnancy.[9] Culdocentesis is a painful, invasive, nonspecific test that adds little if the above test results are available quickly and accurately. A hemodynamically unstable patient with fluid found in the peritoneal cavity by ultrasonography needs prompt surgical treatment whether or not blood is found on culdocentesis. The presence of blood on culdocentesis in a hemodynamically stable patient does not obviate expectant management (transiently bleeding corpus luteum cyst) or medical or laparoscopic management in appropriate patients.

The cornerstones of the early diagnosis of ectopic pregnancy remain a high index of suspicion, sensitive quantitative hCG assay, and transvaginal pelvic ultrasonography. The widespread use of existing diagnostic

and therapeutic techniques could markedly decrease the adverse effects of ectopic pregnancy on women's health.

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Government and Academic Health Science Centers

THIS ISSUE of THE WESTERN JOURNAL OF MEDICINE contains a thoughtful analysis of the many ways in which the national government interacts with and influences the functions of academic health science centers in the United States.[1] The authors, as seasoned senior officers of the Association of American Medical Colleges (AAMC), are exceptionally well informed about these interactions. In fact, it is not by happenstance that the AAMC moved its headquarters from Chicago to Washington, DC, some years ago. The groves of academe, at least in medicine, are no longer tranquil sites for detached scholarship. The imperatives of public policy increasingly intrude, seduce, and command, and the pace of these incursions is accelerating.

This is perhaps not surprising. Academic health science centers are unique in the university in that they are directly involved in running a major industry, that of health care. In all of its other activities the university maintains a well-defined boundary between its academic activities and the workaday world beyond. Schools of medicine, however, participate directly in the industry of health care; it is impossible to ascertain a phase transition between those of their activities that are "academic" and those that are not.

"The health of all the people is really the foundation upon which all their happiness and all their powers as a state depend." Few would dispute the validity of this spacious statement by Disraeli. Nevertheless, the responsibility of the government in assuring access to health care has been accepted fitfully and by slow accretion in this country, much more slowly than in any other so-called developed countries of the world. We are currently lurching further along that pathway with all of the noise and turmoil of the political process. Along with the rest of the medical care system, academic health science centers are being buffeted in this transition, as has been well documented in the review by Petersdorf and Turner.

Academic health science centers educate the next generation of health professionals, directly supply patient care, conduct biomedical research, and render community service. The range of these activities mandates large and complex organizations, with uneasy mingling of the function of the university and of the health care industry. Academic health science centers are therefore highly susceptible to changes in policy and resource allocations in either the university or in the public arena. This vulnerability underlies the choice of title for the current review, "Academe and Government—Firm Link or Broken Reed?" Clearly the link is not firm, but perhaps the reed is only bent rather than broken. Let us hope that it maintains its resiliency to spring back.

A key role of academic health science centers is to conduct biomedical research. Biomedical research is patient care one step removed. In recognition of this, the government allocates approximately $10 billion a year for the support of research, about $40 a year for each citizen. This is a form of national defense, not against external adversaries, but against the implacable, internal adversaries of disease and disability that affect us all, now or in the future. Is it enough? The answer is of necessity a subjective one.

The investment has been enough to ensure the supremacy of the United States in the revolution in biological science that has characterized the last half of the 20th century and in the application of that science to the study of human diseases. The secrets of DNA, formerly locked in nuclear silence, can now be read as an antique and universal language that spells out the structure and function of all living things. Almost weekly, reports appear that elucidate the pathogenesis of genetic disorders as misprints, omissions, or even stuttering in that language of purine and pyrimidine bases strung along a sugar phosphate backbone. A single scientific discovery, that of recombinant DNA technology, has not only revolutionized biology, it has spawned a whole new industry. The annual economic activity of that biotechnology industry alone will shortly exceed the total government investment in biomedical research over the past decade. The return on the national investment in research has clearly been a magnificent achievement and a splendid legacy for the future.

Is it enough? Even in the face of these past prodigies, there is a serious current crisis in biomedical research. We have educated a new generation of basic scientists and physician-scientists who are poised to exploit the opportunities of the new biological sciences. Now, however, the success rate for funding projects that have been approved by stringent peer review as being scientifically meritorious has fallen discouragingly low, often less than one in five. Opportunities are being lost or delayed. Only slightly more than 1% of the national health care budget is being spent to "improve the product," that of health sci-